

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning at page 17, lines 10-19, with the following amended paragraph:

FIG. 1. Schematic diagram of gene activation events described herein. The activation construct is transfected into cells and allowed to integrate into the host cell chromosomes at DNA breaks. If breakage occurs upstream of a gene of interest (e.g., Epo), and the appropriate activation construct integrates at the break such that its regulatory sequence becomes operably linked to the gene of interest, activation of the gene will occur. Transcription and splicing produce a chimeric RNA molecule containing exonic sequences from the activation construct and from the endogenous gene. Subsequent translation will result in the production of the protein of interest. Following isolation of the recombinant cell, gene expression can be further enhanced via gene amplification. The polyA tail is set forth is SEQ ID NO:33.

Please replace the paragraph beginning at page 21, lines 6-17, with the following amended paragraph:

FIG. 13. Illustration depicting two transcripts produced from the integrated vectors described in FIGS. 12A-12G. DNA strands are depicted as horizontal lines. Vector DNA is shown as a black line. Endogenous genomic DNA is shown as a grey line. Rectangles depict exons. Vector-encoded exons are shown as open rectangles, while endogenous exons are shown as shaded boxes. S/D denotes a splice donor site. Following integration, the vector encoded promoters activate transcription of the endogenous gene. Transcription resulting from the upstream promoter produces a spliced RNA molecule containing the vector encoded exon joined to the second and subsequent exons from an endogenous gene. Transcription from the downstream promoter, on the other hand, produces a transcript containing the sequences downstream of the integrated DNA joined to exon I and the subsequent exons from an endogenous gene. The polyA tail is set forth in SEQ ID NO:33.

Please replace the paragraph beginning at page 26, lines 6-25, with the following amended paragraph:

FIGS. 23A-23D. Example of a multi-Promoter/Activation Exon Vector. Each vector is illustrated schematically in its linearized form. Each horizontal line represents a DNA molecule. The arrows denote promoter sequences. Boxes indicate exons. Hatched boxes indicate untranslated regions. It is understood that the exons on these vectors may be untranslated, or may contain a start codon and additional codons as described herein. The following designations were used: splice donor site (S/D), vector promoter #1 (VP #1), vector promoter #2 (VP #2), vector promoter #3 (VP #3), and vector promoter #4 (VP #4). Individual vector activation exons are designated A, B, C, and D (SEQ ID NOS: 29-32, respectively). Each activation exon may contain a different structure. The structure of each activation exon and its flanking intron are shown below. It is understood, however, that any activation exon described herein, may be used on these vectors, in any combination and/or order, including exons that encode signal sequences, partial signal sequences, epitope tags, proteins, portions of proteins, and protein motifs. Any of the exons may lack a start codon. In addition, while not illustrated in these examples, these vectors may contain a selectable marker and/or any amplifiable marker. The selectable marker may contain a poly (A) signal or a splice donor site. When present, the splice donor site may be located upstream or downstream of the selectable marker. Alternatively, the selectable marker may not be operably linked to a poly (A) signal and/or a splice donor site.

Please replace the paragraph beginning at page 29, line 19, with the following amended paragraph:

FIGS. 2A-29B. Nucleotide sequence of pRIG14. (SEQ ID NO: 21).

Please replace the paragraph beginning at page 29, line 20, with the following amended paragraph:

FIGS. 30A-30C. Nucleotide sequence of pRIG19. (SEQ ID NO.: 22).

Please replace the paragraph beginning at page 29, line 21, with the following amended paragraph:

FIGS. 31A-31C. Nucleotide sequence of pRIG20. (SEQ ID NO.: 23).

Please replace the paragraph beginning at page 29, line 22, with the following amended paragraph:

FIGS. 32A-32C. Nucleotide sequence of pRIGad1. (SEQ ID NO.: 24).

Please replace the paragraph beginning at page 29, line 23, with the following amended paragraph:

FIGS. 33A-33D. Nucleotide sequence of pRIGbd1. (SEQ ID NO.: 25).

Please replace the paragraph beginning at page 29, line 24, with the following amended paragraph:

FIGS. 34A-34B. Nucleotide sequence of pUniBAC. (SEQ ID NO.: 26).

Please replace the paragraph beginning at page 29, line 25, with the following amended paragraph:

FIGS. 35A-35B. Nucleotide sequence of pRIG22. (SEQ ID NO.: 27).

Please replace the paragraph beginning at page 30, line 9, with the following amended paragraph:

FIGS. 37A-37C. Nucleotide sequence of pRIG-T. (SEQ ID NO:28).